REMARKS

Reconsideration is respectfully requested. Claims 88-134 are pending. Claim 1-87 have been cancelled. New claims 88-134 have been added. No new matter has been added due to the amendments.

With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

The Applicants note that the claims are now directed to antibodies and immunoadhesins that comprise an amino acid substitution at position 239. That is, the Applicants have withdrawn all claims directed to the other 17 amino acid positions of the claims. All claims now require a 239 substitution. Thus, the burden on the Examiner to examine additional species as species are found allowable has been significantly reduced.

The Applicants believe the newly presented claims 113-134 drawn to methods fall under the original restriction in the present case, dated April 21, 2006, which recited 2 groups (compositions and methods). Upon confirmation by the Examiner that these claims would be considered to be within the original restriction, Applicant will withdraw these claims from further consideration until such time as rejoinder may be appropriate. That is, the Examiner is requested to specifically indicate that the subject matter of new claims 113-34 is patentable distinct from the subject matter of original Group I (claims 1-55, 57-59, and 61-85).

Priority

The Examiner asserts that the priority documents fail to provide support for position 239. The Examiner mistakenly states that only E and R substitutions are disclosed in the priority document.

Applicants respectfully traverse this observation of the Examiner. As explained to the Examiner, the determination of priority on this issue is crucial to the Applicants.

The Applicants respectfully draw the Examiner's attention to Figures 2, 10, 11, of USSN 60/414,433, which clearly shows a variety of variant amino acids at position 239. For example, Figure 2 shows 239E and 239R at row 4 of the first table, and 239K, 239R, 239D, and 239E at row 5 of the second table; Figure 10 shows 239H at row 6 of the table; and Figure 11 shows 239F, 239W and 239Y at rows 13-15 of the table. Moreover, the legend of Figure 10 discloses that: "For each chain A Fc region listed

all amino acids except proline and cysteine were substituted separately." The Legend of Figure 11 discloses that "For each chain A Fc region listed all amino acids except proline and cysteine were substituted separately." Thus USSN 60/414,433 discloses all substitutions except proline and cysteine of the 239 position, include those listed in the tables. Thus, in fact, 17 out of 19 species (e.g. all substitutions except wild type and proline and cysteine) are disclosed in USSN 60/414,433. Applicants submit that this fully supports the genus of variants at position 239.

Accordingly, the Applicants respectfully request an acknowledgement of such priority.

Rejections under 35 U.S.C. §102(b)

Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86 and 87 stand rejected over Presta WO 00/42072 ("*Presta*").

Claims 1-3, 6, 7, 10-14, 16, 18, 19, 21-28, 34, 40, 41, 59, 63, 79, 80, 86 and 87 have been canceled, rendering the rejections moot.

Applicants respectfully submit newly added claims 88- 137 are not anticipated by *Presta*.

Anticipation requires that every limitation of the claim in issue be disclosed, either expressly or inherently, in a single prior art reference. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); M.P.E.P. § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). *Presta* fails to anticipate the claimed invention for the reasons stated below.

***Presta*'s disclosure of position 239 and the separate teaching that amino acids can be substituted do not anticipate the elected substitution species 239D.**

Applicants submit that new claims 88, 89, 91, and 92 (and claims dependent therefrom) are not anticipated by *Presta*.

The Examiner cites *Ex parte* A in support of the 102(b) rejection over *Presta*. Applicants respectfully draw the Examiner's attention to the recent Board of Patent Appeal and Interferences' decision in *Ex parte Watkins* (Appeal 2007-2523). Applicants are mindful that *Ex parte Watkins* is a non-binding opinion. However, Applicants believe that an appeal of the present claims would result in the identical decision by the Board.

In *Watkins*, the independent claim 1 read:

> 1. A composition comprising a variant a parent polypeptide having at least a portion of an Fc region, wherein said variant mediates antibody-dependent cell-mediated cytotoxcity (ADCC) in the presence of effector cells more effectively than said parent polypeptide, wherein said variant comprises a histidine, glutamine or tyrosine amino acid

at position 280 in the Fc region, and wherein said parent polypeptide is an antibody or immunoadhesin.

In *Watkins,* the Examiner relied on Presta (US Patent No. 6,737,056) "*Presta II*" to reject claim 1 and claims dependent therefrom of under 35 U.S.C. §102(e) as being anticipated by *Presta II*.

Specifically, the Examiner based her rejection on the finding that "Presta [II] teaches ... a polypeptide (e.g. antibody or immunoadhesin) comprising a variant Fc region with higher binding affinity to FcγR including FcγRIII and an amino acid substitution at positions such as 280 in the CH2 region for improved antibody –dependent cell-medicate[d] cytotoxicity" and that "Presta [II] defines amino acid residues in a predetermined amino acid sequence with another different amino acid resid[u]e including histidine, glutamine or tyrosine." *Watkins*, at 3. The Examiner also relied on *Ex parte A*, 17 USPQ2d 1716 (BAPAI, 1990) for the rejection.

The Board reversed the rejection. Specifically, the Board rejected the Examiner's reliance on *Presta* II's definition of amino acid substitution which lists twenty standard amino acids, because such definition "does not describe substituting the amino acid at position 280 with any of these twenty amino acids." *Watkins* at 6. Moreover, the Board states:

> [W]e do not agree that Presta [II] provides a specific teaching of substituting the amino acid at position 280 with each of these twenty amino acids and therefore with the three amino acids recited in claim 1. *Id.* at 6.

Here, in the instant Office Action, the Examiner bases the rejection on the disclosures of *Presta* that is similar to the disclosure of Presta II relied upon by the Examiner in *Watkins*, and relied on the similar reading of Ex parte A. Specifically, the Examiner states:

> Presta clearly identifies that position 239 of the Fc region of the parent polypeptide can be substituted with any other amino acid residues including aspartic acid (D) other than the parent residude serine (S) (e.g. pages 14-15). Presta further teaches the preferred substitution for Serine (S) is Threonine (T) (see Table 1 on page 4, in particular).

However, pages 14-15 of *Presta* lists all of the twenty naturally occurred amino acids as potential substitution, the same definition of "amino acid substitution" disclosed in *Presta* II. Thus, identical to *Watkins*, such definition "does not describe substituting the amino acid at position [293] with any of these twenty amino acids."

Therefore, *Presta* does not anticipate the claims. Applicants respectfully request that this ground for rejection be withdrawn and that the additional non-elected species be examined consistent with the election of species requirement.

The polypeptides of claims 88, 90, and 93 (and claims dependent therefrom) comprise an antibody or immunoadhesin of a parent Fc polypeptide that has both a structural and functional limitation. Specifically, the antibody or immunoadhesin a) includes at least one substitution at the position 239, and b) "increases binding affinity to an FcγR as compared to [the] parent Fc polypeptide." A substitution must meet both the structural and functional claim limitations to be within the scope of the claimed invention.

Presta does not teach the claimed species position 239 having the required functional limitation. At page 5, line 32, Presta discloses that a group of modifications that include elected position 239 display "reduced binding to an FcγR." At page 6, line 10, Presta discloses that a group of modifications that include position 239 display "reduced binding to an FcγRIIIa." The best demonstration of this is in Table 6, which discloses the sole substitution at position 239, which was an alanine substitution, 239A. Table 6 shows that 239A has reduced binding affinity to both FcγRIII and FcγRII. Amino acid substitutions that do not result in an Fc variant with increased binding affinity to an FcγR are outside the scope of the claims. Without meeting the positive functional limitation, Presta cannot anticipate the claim.

The claimed polypeptide is also not inherent in the teaching of Presta. To be inherent, the claimed limitation must "necessarily flow" from the teachings of the cited reference. The mere fact that a claimed compound may have the claimed function is insufficient to establish inherent anticipation. See M.P.E.P. § 2163.07(a). As noted above, page 5, line 32 of *Presta* discloses that modifications at position 239 display "reduced binding to an FcγR," page 6, line 10 of *Presta* discloses that modifications at position 239 display "reduced binding to an FcγRIIIa", and Table 6 shows the sole 239 variant, 239A, has decreased binding to both FcγRIII and FcγRII. One of skill in the art would not draw the conclusion that variants at position 239 would "necessarily" result in increased binding; rather, if anything, the opposite inference could be drawn.

Further, *Presta* does not disclose any specific substitution at position 239 that inherently has the claimed functional limitation. As discussed below, *Presta* provides a generalized teaching for making modifications at a large genus of numerous positions in the Fc region. In this context, such a generalized teaching of a genus is not an anticipatory teaching of a specific substitution at a specific position. As such, *Presta* does not teach any substitution at the elected position 239 that inherently "increases binding affinity to an FcγR" as claimed.

Rejections under 35 U.S.C. §102(e)

Claims 1-3, 6, 7, 10-15, 18-27, 34-40, 43, 59 and 63 stand rejected over Presta II (U.S. Patent No. 6,737,056).

Claims 1-3, 6, 7, 10-15, 18-27, 34-40, 43, 59 and 63 have been canceled, rendering the rejection moot.

Applicants respectfully submit newly added claims 88- 137 are not anticipated by *Presta*.

Presta II does not anticipate the claims for the reasons described above in the response to the rejection under 35 U.S.C. §102(b). First, *Presta II* neither expressly nor inherently teaches an antibody or immunoadhesin of a parent Fc polypeptide comprising "an amino acid substitution at position 239,

wherein said antibody or immunoadhesin increases binding affinity to an FcγR as compared to said Fc polypeptide." Second, *Presta II* fails to anticipate the elected substitution species 239D.

As such, the presently claimed invention is not anticipated by *Presta II*. Applicants respectfully request that this ground for rejection be withdrawn.

Conclusion

In light of the above amendments and remarks, Applicants believe that this case is now in condition for allowance. Early notification is respectfully requested. Should there be any remaining issues that remain unresolved, the Examiner is encouraged to telephone the undersigned.

Please direct further questions in connection with this Application to the undersigned at (415) 442-1000.

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